REMARKS

Claims 1-22, 24, 34, 43, 56, and 76 were pending. Claims 3, 4, 22, and 76 were withdrawn from consideration. Claim 16 is cancelled without prejudice by the present Amendment. Claims 1, 2, 5, 6, 12, 13, 15, 17-21, 24, 34, 43, and 56 are amended. Upon entry of these amendments, claims 1, 2, 5-15, 17-21, 24, 34, 43 and 56 will be pending for further consideration.

Claims 1, 2, 5, 6, 12, 13, 17-21, 24 and 43 are amended to recite an "immunostimulatory nucleic acid" with no intention of disclaiming equivalents thereto. Basis for this recitation can be found in the specification at least at pages 38-41.

Claim 15 is amended to recite "an amino acid backbone" with no intention of disclaiming equivalents thereto. Basis for this recitation can be found in the specification at least on page 37, lines 3-4.

Claim 24 is also amended to recite a "surface antigen chosen from a CD22 antigen and a CD19 antigen" with no intention of disclaiming equivalents thereto. Basis for this recitation can be found in the specification at least on page 3, lines 6-10, and page 11, lines 1-15.

Claim 34 is amended to replace the recitation of a "control B cell" with the recitation of a "normal B cell" with no intention of disclaiming equivalents thereto. Basis for this amendment can be found in the specification at least on page 3, lines 11-18, and page 12, lines 8-15.

Claims 1, 34, 43, and 56 are also amended to correct other minor informalities and clarify the claimed subject matter with no intention of disclaiming equivalents thereto. Basis for these amendments can be found at least in the claims as originally filed.

No new claims are presented. Applicants believe that the above-referenced amendments introduce no new subject matter.

Information Disclosure Statements and Forms 1449

Applicants have not yet received copies of two Forms 1449 that were submitted to the U.S. Patent and Trademark Office. Specifically, Applicants have not yet received a copy of a Form 1449 (listing references C122 to C153) that was mailed on September 28, 2001, along with

a supplemental Information Disclosure Statement, copies of references C122 to C153, and a return receipt postcard. The return receipt postcard was stamped as received by the U.S. Patent and Trademark Office on October 1, 2001. In addition, Applicants have not yet received a copy of a Form 1449 (listing references A39 and C154 to C157) that was mailed on September 23, 2002, along with a supplemental Information Disclosure Statement, copies of references A39 and C154 to C157, and a return receipt postcard. This return receipt postcard was stamped as received by the U.S. Patent and Trademark Office on September 30, 2002.

Applicants respectfully request copies of the above-referenced Forms 1449 initialed by the Examiner to indicate that references A39 and C122 to C157 have been considered.

Election of Species

Applicants gratefully acknowledge rejoinder by the Examiner of Groups I and III. Applicants also hereby affirm, as required by the Examiner, their previous election of species i), namely an immunostimulatory CpG nucleic acid. Claims 1, 2, 5-15, 17-21, 24, 34, 43 and 56 are readable on the elected species.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 5-21, 24, 34, 43, and 56 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite or failing to particularly point out and distinctly claim the subject matter the applicant regards as the invention. In response, Applicants have amended claims 1, 2, 5, 6, 12, 13, 15, 17-21, 24, 34, 43, and 56, and cancelled claim 16.

Claims 1, 15, 24, 34, 43, and 56 are amended as described above to correct minor informalities and clarify the claimed subject matter. Applicants submit that these amendments obviate the Examiner's specific rejections of each of these claims and the claims that depend therefrom (see pages 4-5 of the Office Action).

In addition, the Examiner rejected claims 1, 24, 34, and 43 as allegedly lacking an active or positive step (see page 5 of the Office Action). The Examiner relied on *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. Int. 1986) as authority for requiring that the claims recite an active or positive step. Applicants respectfully traverse this rejection, because the present claims

positively recite method steps, unlike the claims that were rejected under 35 U.S.C. § 112, second paragraph, in *Ex parte Erlich.* For example, claim 6 at issue in *Ex parte Erlich* failed to recite a single method step and recited only:

> 6. A process for using monoclonal antibodies of Claim 4 to isolate and purify human fibroblast interferon.

Similarly, claim 7 at issue in *Ex parte Erlich* recited only:

> 7. A process for using monoclonal antibodies of Claim 4 to identify human fibroblast interferon.

In contrast, pending claims 1, 24, 34, and 43 recite the specific steps of administering an immunostimulatory nucleic acid and administering an antibody. Therefore, Applicants submit that these claims recite positive steps that comply with the requirements of *Ex parte Erlich.*

Therefore, Applicants respectfully request that the rejection of claims 1, 2, 5-21, 24, 34, 43, and 56 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 24, 34, 43, and 56 under 35 U.S.C. § 112, first paragraph, for an alleged lack of adequate written description. The Examiner further rejected claims 1, 2, 5-21, 24, 34, 43, and 56 under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement.

Rejections of claim 24 under 35 U.S.C. § 112, first paragraph

a) Written Description:

Claim 24 was rejected under 35 U.S.C. § 112, first paragraph, for a lack of adequate written description. The Office Action alleges on page 6 that "the claim encompasses administration of any nucleic acid which induces the expression of any cancer antigen …" and therefore encompasses "a genus of possibly millions of different nucleic acids considering every possible nucleic acid which could stimulate the expression of any cancer antigen expression …."

Applicants respectfully traverse this rejection to the extent that it is maintained over claim 24 as amended herein. Amended claim 24 recites administering "an immunostimulatory nucleic acid in an effective amount to induce expression of a surface antigen on a cancer cell

surface, wherein the surface antigen is chosen from a CD22 antigen and a CD19 antigen ...." Applicants respectfully submit that the specification as filed discloses the important features of an immunostimulatory nucleic acid. See, for example, the detailed description from line 11 on page 38 through line 18 on page 41. The specification also provides numerous exemplary immunostimulatory nucleic acids in Table 4, on pages 46 through 61.

The Office Action also alleges on page 7 that claim 24 "encompasses inducing the expression of any cancer antigen (including new antigens that have not yet been identified) in any type of cancer cell." Applicants respectfully submit that this rejection is obviated by the recitation of a surface antigen "chosen from a CD22 antigen and a CD19 antigen" in amended claim 24. These antigens are disclosed in the specification at least on page 11, lines 1-15.

Furthermore, Applicants respectfully submit that the written description requirement is satisfied when there is "sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing." *Moba B.V., v. Diamond Automation Inc.*, 66 USPQ2d 1429, 1439 (Fed Circ. 2003). The written description requirement "does not require a particular form of disclosure," instead it requires that "one of skill could determine from the specification that the inventor possessed the invention at the time of filing." *Id.* Applicants submit that in view of the present claim amendments, one of ordinary skill would readily determine that Applicants possessed the invention of claim 24 at the time the application was filed.

Therefore, Applicants respectfully request reconsideration and withdrawal of the written description rejection of claim 24 under 35 U.S.C. § 112, first paragraph.

b) Enablement:

Claim 24 was also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office Action alleges on page 8 that claim 24 "encompasses administration of any nucleic acid which induces the expression of any cancer antigen in a any type of cancer cell" and that "additional experimentation is required in order for one of skill in the art to be able to make and use the invention with a reasonable expectation of success." Applicants respectfully traverse this rejection to the extent that it is maintained over claim 24 as amended herein. As

discussed above, amended claim 24 recites an "immunostimulatory nucleic acid" and a surface antigen "chosen from a CD22 antigen and a CD19 antigen." Applicants submit that the specification provides detailed guidance related to the use of immunostimulatory nucleic acids and the above-referenced surface antigens. Applicants explain that their invention is based in part on the "discovery that immunostimulatory nucleic acids are capable of upregulating expression of certain target antigens on the surface of cancer cells …." Applicants further explain that the invention provides "therapies using immunostimulatory nucleic acids in combination with specific antibodies …." See the specification at least on page 11, lines 1-15. As discussed above, Applicants specifically disclose the use of an anti-CD22 antibody or an anti-CD19 antibody. Applicants also describe methods for administering immunostimulatory nucleic acids and antibodies. See the specification at least on pages 63-69. Therefore, Applicants submit that one of ordinary skill could use the present disclosure to practice the method of amended claim 24 without undue experimentation.

Applicants note that the Examiner refers to the written description guidelines in the context of the enablement rejection on page 8 of the Office Action. Applicants respectfully submit that the written description requirement is satisfied for claim 24 as discussed above. Applicants further submit that the enablement analysis is separate from the written description analysis and should focus on whether one of ordinary skill in the art could practice the invention as claimed without undue experimentation. In view of the high level of skill in the art, Applicants submit that their disclosure of immunostimulatory nucleic acids that "actually cause the induction of specific antigens CD20, CD19, and CD22, each of which can be targeted by specific antibody therapies" is sufficient to enable claim 24. The disclosure is further enabling, because it also provides detailed guidance on how to implement the claimed invention as discussed above.

Therefore, Applicants respectfully request that the rejection of claim 24 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections of claim 34 under 35 U.S.C. § 112, first paragraph

a) Written Description:

Claim 34 was rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate written description. The Office Action alleges on page 10 that "there is no disclosure in the specification or art which indicates that the disclosed species of immunostimulatory nucleic acid would stimulate expression of every possible B-cell cancer antigen, in particular there is no indication that the immunostimulatory nucleic acids disclosed will be capable of upregulating the expression of any unidentified antigens." Applicants respectfully traverse this rejection. As a threshold matter, Applicants respectfully submit that claim 34 does not require that an immunostimulatory nucleic acid stimulate expression of every possible B-cell antigen. As explained above, the invention is based in part on the discovery that an immunostimulatory nucleic acid can induce the expression of a cell surface antigen in a B-cell cancer. The invention of claim 34 involves treating a lymphoma by "identifying a surface antigen which is not expressed or which is expressed on the surface of a B cell in an amount lower than that of a normal cell" and "administering an immunostimulatory nucleic acid in an effective amount to upregulate expression of the surface antigen" along with "an antibody specific for the surface antigen." In this invention, only one surface antigen needs to be upregulated by an immunostimulatory nucleic acid. While it may upregulate several antigens, the immunostimulatory nucleic acid does not need to upregulate every B-cell antigen as suggested in the Office Action. Applicants submit that this feature of the invention is clearly disclosed. See, for example, lines 11-18 on page 3 of the specification.

Applicants respectfully submit that claim 34 satisfies the written description requirement which "does not require a particular form of disclosure," but instead requires that "one of skill could determine from the specification that the inventor possessed the invention at the time of filing" as discussed above. Indeed, the specification discloses the common features of the antigens encompassed by claim 34: namely that each antigen is a "surface antigen"; each antigen "is not expressed" or "is expressed on the surface of a B cell in an amount lower that that of a normal B cell;" and the expression of each antigen can be upregulated by administering an "immunostimulatory nucleic acid." Applicants also provide a detailed description of useful

immunostimulatory nucleic acids as discussed above. Therefore, Applicants submit that one of skill in the art would recognize that Applicants were in possession of the invention at the time of filing.

Therefore, Applicants respectfully request that the written description rejection of claim 34 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

b) Enablement:

Claim 34 was also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office Action alleges on page 11 that "[I]in order to make and use the claimed invention, a number of antigens which would be representative of every B-cell lymphoma antigen would have to be identified." Applicants respectfully traverse this rejection. Applicants wish to clarify that in order to practice the claimed method and treat a particular lymphoma, one of ordinary skill need only identify for that lymphoma a single antigen having the common features recited in claim 34. Applicants disclosure provides the necessary guidance for identifying such an antigen and administering an immunostimulatory nucleic acid in combination with an antibody specific for that antigen. Applicants respectfully submit that given the level of skill in the art, no undue experimentation is required to practice the invention of claim 34.

The Examiner again refers to the written description guidelines in the context of this enablement rejection. The examiner also stated that it "would require a tremendous amount of experimentation" to identify "the necessary attributes/features common to the B-cell lymphoma surface antigens and nucleic acid molecules which upregulate their expression." However, as discussed above, Applicants have provided common features sufficient to satisfy the written description requirement. In view of these common features, and the additional guidance provided in the specification, Applicants respectfully traverse the Examiner's assertion regarding "a tremendous amount of experimentation." While some experimentation may be necessary, this does not negate enablement, and Applicants submit that any necessary experimentation would not be undue in view of the detailed description and guidance provided in the specification.

Therefore, Applicants respectfully request that the enablement rejection of claim 34 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections of claim 43 under 35 U.S.C. § 112, first paragraph

a) Written Description:

Claim 43 was rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate written description. On pages 12-13 of the Office Action, the Examiner alleges that "there is no disclosure in the specification or in the art which indicates that the disclosed species would upregulate expression of every possible antigen in a lymphoma cell that is resistant to antibody treatment. In particular there is no indication that the described species would be capable of upregulating the expression of any unidentified antigens." Applicants respectfully traverse this rejection. Applicants wish to clarify that claim 43 does not require that a single species of immunostimulatory nucleic acid upregulate every antigen in a lymphoma cell that is resistant to antibody treatment. Claim 43 is drawn to a method for treating a lymphoma that is resistant to a particular antibody therapy directed at a particular surface antigen. According to claim 43, the resistant lymphoma is treated by administering a) the antibody that is specific for the surface antigen and b) an immunostimulatory nucleic acid "in an effective amount to upregulate expression of the surface antigen." An important basis for the invention is the discovery that an immunostimulatory nucleic acid can upregulate the expression of a surface antigen on a B cell, and that this upregulated surface antigen can be used as a target for an effective antibody therapy. According to the invention, a different immunostimulatory nucleic acid could be used to upregulate the expression of a different antigen. Applicants submit that the specification clearly discloses these aspects of the invention, and provides common features for useful antigens and immunostimulatory nucleic acids, as discussed above. Accordingly, Applicants submit that one of skill in the art would recognize that Applicants possessed this invention at the time the application was filed.

Therefore, Applicants respectfully request that the written description rejection of claim 43 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

b) Enablement:

Claim 43 was also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. On pages 13-14 of the Office Action, the Examiner states that "[I]in order to make and use the claimed invention, a number of antigens and nucleic acid molecules which would be

representative of all species of antigens and nucleic acids would have to be identified." The Examiner again refers to the written description guidelines in the context of this enablement rejection. Applicants respectfully traverse this rejection. Applicants again submit that the specification satisfies the written description guidelines for claim 43, and discloses common features of useful antigens and immunostimulatory nucleic acids, as discussed above. Applicants further submit that enablement does not require the disclosure of a representative number of species. The number of disclosed species can be considered when evaluating enablement. However, the inquiry should focus on whether one of ordinary skill could practice the invention without undue experimentation. Applicants submit that claim 43 is enabled, because Applicants have provided the discovery that an immunostimulatory nucleic acid can be administered to a subject to upregulate expression of an antigen on a lymphoma, thereby allowing the lymphoma to be treated with an antibody specific for that antigen. See, for example, lines 19-24 on page 3 of the specification. In view of the level of skill in the art, Applicants submit that this disclosure alone should be enabling. However, Applicants also provide details concerning the features of useful immunostimulatory nucleic acids, useful antigens and antibodies, and useful methods of administration.

Therefore, Applicants respectfully request that the enablement rejection of claim 43 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections of claim 56 under 35 U.S.C. § 112, first paragraph

a) Written Description:

Claim 56 was rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate written description. On page 15 of the Office Action, the Examiner alleges that "there is no disclosure indicating any common attributes or structural elements which are common to all surface antigens on all cancer cells." The Examiner concludes that " the claim encompasses antigens and antibodies which are not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Applicants respectfully traverse this rejection to the extent that it is maintained over claim 56 as amended, because the

specification discloses the common features of the antibodies encompassed by claim 56: namely that each antibody is specific for a "surface antigen;" and each antibody is an antibody of IgG1 isotype. These features are disclosed at least on page 4, lines 5-9, on page 29, lines 11-14, and in Table 2 on pages 29-32 of the specification as filed. Applicants further submit that these features are sufficient to satisfy the written description requirement for claim 56.

Therefore, Applicants respectfully request that the written description rejection of claim 56 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

b) Enablement:

Claim 56 was also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. On pages 16-17 of the Office Action, the Examiner again refers to the written description guidelines to reject the claim for lack of enablement. The Examiner also alleges that "a number of antigens which would be representative of every possible antigen on every human cancer cell would have to be identified." Applicants respectfully traverse this rejection. As discussed above, Applicants have satisfied the written description guidelines, and have provided common features of useful antibodies, antigens, and immunostimulatory nucleic acids. One of ordinary skill in the art could practice the invention using a single antibody and a single immunostimulatory nucleic acid having these common features without undue experimentation.

Therefore, Applicants respectfully request that the enablement rejection of claim 56 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections of claim 1, 2, and 5-21 under 35 U.S.C. § 112, first paragraph

Enablement:

Claims 1, 2, and 5-21 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. On pages 16-23 of the Office Action, the Examiner refers to several of the factors described by the court in *In re Wands*, 8 USPQ2d 1400 (Fed. Circ. 1988). Applicants respectfully traverse these rejections to the extent that they are maintained over the claims as amended. Applicants address each of the factors discussed by the Examiner in the following paragraphs.

The nature of the invention/The breadth of the claims:

The amended claims relate to administering a combination of an immunostimulatory nucleic acid that upregulates CD20 expression and an anti-CD20 antibody, both of which are disclosed in the specification as filed.

The unpredictability of the art and the state of the prior art:

On page 18 of the Office Action, the Examiner alleges that the claims encompass methods of gene therapy. Applicants have amended the claims to recite an "immunostimulatory nucleic acid." Accordingly, Applicants submit that claims 1, 2, and 5-21 do not encompass a method of gene therapy as described by the Examiner.

On pages 19-20 of the Office Action, the Examiner describes features of allegedly useful immunostimulatory nucleic acids. Applicants submit that the specification provides a detailed description of useful immunostimulatory nucleic acids according to the invention. See at least pages 38-41 of the specification.

On page 20 of the Office Action, the Examiner alleges that there is a "high degree of unpredictability of preventing cancer." Applicants submit that the specification teaches that cancer can be treated by "preventing growth of a cancer cell by decreasing or slowing the rate of growth, by inhibiting growth altogether, or by killing or inducing apoptosis of the cancer cell" (page 32, lines 3-5). Accordingly, methods of the invention can prevent cancer via antibody-dependent cellular cytotoxicity as described at least on page 11, lines 1-15, of the specification as filed. Therefore, Applicants submit that the issues relating to "preventing genetic mutation, and immortalization," raised on page 21 of the Office Action, are not relevant for amended claims 1, 2, and 5-21.

Working examples and guidance in the specification:

As discussed in detail above, the specification provides guidance on CD20 antibodies and immunostimulatory nucleic acids that upregulate expression of CD20 antigens. The

specification also provides a working example of the upregulation of CD20 expression in response to an immunostimulatory nucleic acid. See, for example, Example 1 on pages 73-75.

Quantity of experimentation:

Applicants submit that one of ordinary skill can practice the invention using antibodies and immunostimulatory nucleic acids disclosed in the specification. Applicants further submit that the guidance provided in the specification allows one of ordinary skill to identify additional immunostimulatory nucleic acids in order to practice the claimed invention with a reasonable expectation of success.

The Examiner's remarks, on page 22 of the Office Action, relating to "delivering a nucleic acid encoding an tumor antigen" are obviated by the recitation of an "immunostimulatory nucleic acid" in the amended claims.

Level of skill in the art:

Applicants agree with the Examiner that the level of skill in the art is high.

In conclusion, Applicants submit that amended claims 1, 2, and 5-21 are enabled by the specification as filed. Therefore, Applicants respectfully request that the enablement rejection of claims 1, 2, and 5-21 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 102(b)

The Examiner rejected claims 1, 2, 5, 7, 13, 14, 16-19, and 21 under 35 U.S.C. § 102(b) as being anticipated by Wooldridge et al. (1997) *Blood* 89:2994-8 (hereinafter referred to as "Wooldridge"). Applicants respectfully disagree with the Examiner's rejection, because the cited reference does not teach what the Examiner says it teaches. Specifically, the Examiner asserts that monoclonal antibody MS11G6 is an anti-CD20 antibody. However, as disclosed in the last paragraph on page 2994 of Wooldridge and in Example 3 of the instant application, MS11G6 is not an anti-CD20 antibody but is instead an anti-idiotype antibody, i.e., an anti-antibody antibody. Wooldridge specifically discloses that the idiotype expressed by the surface

IgM of 38C13 cells is the antigen recognized by MS11G6. Because claim 1 involves use of an anti-CD20 antibody and Wooldridge does not teach the use of an anti-CD20 antibody as alleged by the Examiner, Wooldridge does not anticipate claim 1 or any of claims 2, 5, 7, 13, 14, 16-19, and 21 which depend from claim 1. Therefore, Applicants respectfully request that the rejection of claims 1, 2, 5, 7, 13, 14, 16-19, and 21 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 102(a)

The Examiner rejected claims 1, 2, 5, 7, 12-14, and 16-21 under 35 U.S.C. § 102(a) as being anticipated by Warren et al. (2000) *Clin Lymphoma* 1:57-61 (hereinafter referred to as "Warren"). Applicants respectfully disagree with the Examiner's rejection, because the cited reference does not teach what the Examiner says it teaches. Specifically, the Examiner asserts that monoclonal antibody MS11G6 used in Warren is an anti-CD20 antibody. However, as noted above, MS11G6 is not an anti-CD20 antibody. Because claim 1 involves use of an anti-CD20 antibody and Warren does not teach the use of an anti-CD20 antibody as alleged by the Examiner, Warren does not anticipate claim 1 or any of claims 2, 5, 7, 12-14, and 16-21 which depend from claim 1. Therefore, Applicants respectfully request that the rejection of claims 1, 2, 5, 7, 12-14, and 16-21 under 35 U.S.C. § 102(a) be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected claims 5, 6, 8-12 and 20 under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Krieg et al. (1998) *BioDrugs* 10:341-6 (hereinafter referred to as "Krieg"). Applicants respectfully traverse this rejection, because Wooldridge and Krieg both fail to teach or suggest using an anti-CD20 antibody. Therefore, the combination of these references fails to disclose an element of the rejected claims: namely the step of administering an anti-CD20 antibody. Accordingly, these references cannot form the basis for continued rejection of claims 5, 6, 8-12 and 20 under 35 U.S.C. § 103(a). Therefore, Applicants respectfully request reconsideration and withdrawal of these rejections.

The Examiner also rejected claims 6 and 8-11 under 35 U.S.C. § 103(a) as being unpatentable over Warren in view of Krieg. Applicants respectfully traverse this rejection, because Warren and Krieg both fail to teach or suggest using an anti-CD20 antibody. Therefore, the combination of these references fails to disclose an element of the rejected claims: namely the step of administering an anti-CD20 antibody. Accordingly, these references cannot form the basis for continued rejection of claims 6 and 8-11 under 35 U.S.C. § 103(a). Therefore, Applicants respectfully request reconsideration and withdrawal of these rejections.

The Examiner also rejected claim 24 as being unpatentable under 35 U.S.C. § 103(a) over Wooldridge in view of Goldenberg (WO 98/423678) (hereinafter referred to as "Goldberg"). Applicants respectfully disagree with the Examiner, because there is no motivation to combine the teachings of Woolridge and Goldenberg. Wooldridge did not recognize any direct effect of CpG oligonucleotides on lymphoma cells (see the last paragraph on page 2997). Rather, Wooldridge teaches that CpG oligonucleotides enhanced antibody-dependent cellular cytotoxicity (ADCC) by activating natural killer (NK) and other effector cells. Wooldridge offered as mere speculation that "it is possible the CpG ODN induced changes in the tumor cells that rendered them more sensitive to MoAb therapy." (*Ibid.*) Wooldridge makes no direct reference to any of CD19, CD20, or CD22. Furthermore, as discussed above, Wooldridge teaches the use of CpG with an antibody directed against an anti-idiotype antigen distinct from CD20, CD19, and CD22. Applicants submit that Wooldridge does not teach or suggest that the anti-idiotype antibody could be replaced by an antibody specific for CD20, CD19, or CD22.

Goldenberg indeed appears to teach a method for treating B-cell malignancies by administering an anti-CD22 antibody. However, Goldenberg fails to suggest combining an anti-CD22 antibody with an immunostimulatory nucleic acid. Goldenberg also fails to teach or suggest that the expression of a surface antigen on a B cell can be upregulated by an immunostimulatory nucleic acid.

Therefore, Applicants submit that the Examiner has failed to provide sufficient evidence for a *prima facie* obviousness rejection which requires at least some motivation in the prior art to combine the cited references. Neither Wooldridge nor Goldenberg provide a specific suggestion to combine the administration of an anti-CD22 or anti-CD19 antibody with the administration of

an immunostimulatory nucleic acid. Moreover, neither reference recognizes the effect of an immunostimulatory nucleic acid on antigen expression by a cancer cell. Therefore, these references fail to provide the necessary motivation to combine their teachings.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 24 under 35 U.S.C. § 103(a).

SUMMARY

Applicants believe that claims 1, 2, 5-15, 17-21, 24, 34, 43, and 56 are in condition for allowance. Applicants respectfully request that withdrawn claims 3 and 4 be reconsidered and allowed along with generic claim 1, in accordance with 37 C.F.R. §1.141. An early and favorable response is earnestly solicited. The Examiner is invited to contact the undersigned by telephone to discuss any remaining issues of patentability.

Respectfully submitted,

Patrick R.H. Waller, Reg. No.: 48,418
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210-2211
(617) 720-3500

Docket No. C01039.70052.US
Date: July 9, 2003
x07/09/03